Amendment

In the Claims:

Please amend the following claims as shown in the Marked-Up Version with Markings to Show the Changes and the Clean Set of Claims attached hereto:

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100. (Third Amended) A method of regulating expression of a desired protein or RNA in an animal, the method comprising:

administering to the animal a pharmacological dose of a ligand, wherein the ligand is an antagonist for a non-mutated receptor protein,

wherein the animal contains:

(a) a first nucleic acid cassette comprising a coding sequence of a molecular switch comprising a mutated receptor protein, wherein the mutated receptor protein comprises:

a DNA binding domain which binds a promoter transcriptionally linked to a target gene;

a mutated steroid hormone receptor superfamily ligand binding domain which is distinct from a naturally occurring ligand binding domain, has an amino acid alternation in C-terminus and binds to the ligand;

a transactivation domain which causes transcription from the promoter when the molecular switch is bound to the promoter and the ligand; and

(b) a second nucleic acid cassette comprising a nucleic acid encoding the target gene,

wherein administration of the ligand regulates expression of the desired protein or RNA from the target gene.

101. (Amended) The method of claim 100, wherein the mutated steroid hormone superfamily receptor ligand binding domain is selected from the group consisting of estrogen, progesterone, androgen, Vitamin D, COUP-TF, cis-retinoic acid, Nurr-1, thyroid hormone, mineralocorticoid, glucocorticoid-alpha, glucocorticoid-beta, and orphan receptor ligand binding domains.

102. (Twice Amended) The method of claim 100, wherein the mutated receptor protein is a mutated progesterone receptor and the DNA binding domain is a GAL-4 DNA binding domain.

103. (Twice Amended) The method of claim 100, wherein the nucleic acid encoding the desired protein is transcribed to produce an mRNA molecule that is translated to produce the desired protein after the animal is given the pharmacological dose of the ligand.

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104. (Amended) The method of claim 100, wherein the first nucleic acid cassette and the second nucleic acid cassette in the animal are on separate plasmids.

105. (Amended) The method of claim 100, wherein the DNA binding domain is a natural DNA binding domain, a non-native DNA binding domain, or, a modified DNA binding domain.

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107. (Twice Amended) The method of claim 100, wherein the animal is a mammal. (Amended) The method of claim 107, wherein the mammal is a human.

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114. (Amended) The method of claim 100, wherein the mutated steroid hormone superfamily receptor ligand binding domain binds to a compound selected from the group consisting of non-natural ligands, non-native hormones and anti-hormones.

115. (Amended) The method of claim 100, wherein the DNA binding domain is a GAL-4 DNA binding domain, a virus DNA binding domain, an insect DNA binding domain, or a non-mammalian DNA binding domain.

116. (Amended) The method of claim 100, wherein the transactivation domain is selected from the group consisting of VP-16, TAF-1, TAF-2, and TAU-2.

117. (Amended) The method of claim 116, wherein the transactivation domain comprises a TAF-1 transactivation domain.

118. (Amended) The method of claim 100, wherein the transactivation domain is a VP-16 transactivation domain and wherein the DNA binding domain is a GAL-4 DNA binding domain.

119. (Amended) The method of claim 100, wherein the transactivation domain is a TAF-1 transactivation domain and wherein the DNA binding domain is a GAL-4 binding domain.

120. (Amended) The method of claim 100, wherein the molecular switch is tissue specific.

121. (Amended) The method of claim 120, wherein the tissue specificity of the molecular switch is controlled by a tissue-specific transactivation domain.

123. (Twice Amended) The method of claim 100, wherein the alternation is a deletion of carboxyl terminal amino acids in the mutated steroid hormone receptor superfamily ligand binding domain.

127. (Amended) The method of claim 100, wherein the ligand is an endogenous ligand for the mutated steroid hormone receptor.

129. (Twice Amended) The method of claim 100, wherein the ligand is 11 beta-(4-dimethylaminophenyl)-17 beta-hydroxy-17 alpha-propinyl-4,9-estradiene-3-one.

131. (Amended) The method of claim 100, wherein the ligand requires conversion to an active form in an end organ.

132. (Amended) The method of claim 100, wherein the ligand has a side chain which increases or restricts solubility, membrane transfer or target organ accessibility.

133. (Twice Amended) The method of claim 101, wherein the mutated steroid receptor superfamily ligand binding domain is a Vitamin D ligand binding domain.

134. (Twice Amended) The method of claim 133, wherein the mutated receptor is activated when bound by the ligand 24,25-dihydroxy-Vitamin D.

135. (Twice Amended) A method of regulating an expression from a desired protein or RNA in an animal comprising:

administering to the animal a pharmacological dose of a ligand that activates a molecular switch encoded by a first expression cassette comprised in the animal, wherein the activation of the molecular switch results in the expression of the desired protein or RNA from a second expression cassette comprised in the animal, wherein the molecular switch comprises a

mutated steroid hormone superfamily receptor ligand binding domain which is activated by the ligand which is not a native ligand for a corresponding wild type steroid hormone superfamily receptor ligand binding domain.

136. (Amended) The method of claim 135, wherein the mutated steroid hormone superfamily receptor ligand binding domain is the ligand binding domain of a steroid hormone superfamily receptor selected from the group consisting of: estrogen; progesterone; glucocorticoid-α; glucocorticoid-β; mineralcorticoid; androgen; thyroid hormone; retinoic acid; retinoid X; Vitamin D; COUP-TF; ecdysone; Nurr-1 and orphan receptors.

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137. (Amended) The method of claim 136, wherein the mutated steroid hormone superfamily receptor ligand binding domain is a mutated progesterone ligand binding domain and the ligand is an anti-progestin.

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140. (Amended) The method of claim 135, wherein the molecular switch comprises a mutated steroid hormone receptor superfamily ligand binding domain operably attached to a DNA binding domain selected from the group consisting of: a GAL-4 DNA binding domain; a viral DNA binding domains; an insect DNA binding domains; and a non-mammalian DNA binding domains.

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142. (Amended) The method of claim 135, wherein the expression is up-regulated.

143. (Amended) The method of claim 135, wherein the expression is down-regulated.

Please add the following new claims as shown in the Clean Set of Claims attached hereto:

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144. (New) A method of regulating a transient expression of a desired protein or RNA in an animal *in vivo*, the method comprising:

administering to the animal a pharmacological dose of a ligand, wherein the ligand is an antagonist for a non-mutated steroid hormone receptor protein,

wherein the animal comprises:

(a) a first nucleic acid cassette comprising a coding sequence of a molecular switch comprising a mutated receptor protein, wherein the mutated receptor protein comprises:

a DNA binding domain which binds a promoter transcriptionally linked to a target gene;

a mutated steroid hormone receptor superfamily ligand binding domain which is distinct from a naturally occurring ligand binding domain, has an alternation in C-terminal amino acids and binds to the ligand;

a transactivation domain which causes a transcription from the promoter when the molecular switch is bound to the promoter and the ligand; and

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(b) a second nucleic acid cassette comprising the target gene transcriptionally linked to the promoter, wherein administration of the ligand regulates expression of the desired protein or RNA in the animal.

145. (New) The method of claim 144, wherein the mutated steroid hormone superfamily receptor ligand binding domain is selected from the group consisting of estrogen, progesterone, androgen, Vitamin D, COUP-TF, cis-retinoic acid, Nurr-1, thyroid hormone, mineralocorticoid, glucocorticoid-alpha, glucocorticoid-beta, and orphan receptor ligand binding domains.

146. (New) The method of claim 144 wherein the mutated receptor protein is a mutated progesterone receptor and the DNA binding domain is a non-steroid hormone DNA binding domain

147. (New) The method of claim 144, wherein the first nucleic acid cassette and the second nucleic acid cassette in the animal are on separate plasmids.

148. (New) The method of claim 144, wherein the DNA binding domain is a natural DNA binding domain, a non-native DNA binding domain, or, a modified DNA binding domain.

149. (New) The method of claim 144, wherein the animal is a mammal.

150. (New) The method of claim 149, wherein the mammal is a human.

151. (New) The method of claim 144, wherein the DNA binding domain is a Gal-4 DNA binding domain.

152. (New) The method of claim 144, wherein the mutated steroid hormone receptor ligand binding domain binds a compound selected from the group consisting of 5α-pregnane-3,20-dione; 11β-(4-dimethylaminophenyl)-17β-hydroxy-17α-propinyl-4,9-estradiene-3-one; 11β-(4-dimethylaminophenyl)-17α-hydroxy-17β-(3-hydroxypropyl)-13α-methyl-4,9-gonadiene-3-one; 11β-(4-acetylphenyl)-17β-hydroxy-17α--(1-propinyl)-4,9-estradiene-3-one; 11β-(4-dimethylaminophenyl)-17β-hydroxy-17-α--(3-hydroxy-1 (Z)-propenyl-estra-4,9-diene-3-one; (7β,11β,17β)-11-(4-dimethylaminophenyl)-7-methyl-4',5'-dihydrospiro(ester-4,9-diene-17,2'(3'H)-furan)-3-one; (11β,14β,17α)-4',5'-dihydro-11-(4-dimethylaminophenyl)- (spiroestra-4,9-diene-17,2'(3'H)-furan)-3-one.

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153. (New) The method of claim 144, wherein the mutated steroid hormone superfamily receptor ligand binding domain binds to a compound selected from the group consisting of non-natural ligands, non-native hormones and anti-hormones.

154. (New) The method of claim 144, wherein the DNA binding domain is a GAL-4 DNA binding domain, a virus DNA binding domain, an insect DNA binding domain, or a non-mammalian DNA binding domain.

155. (New) The method of claim 144, wherein the transactivation domain is selected from the group consisting of VP-16, TAF-1, TAF-2, and TAU-2.

156. (New) The method of claim 155, wherein the transactivation domain comprises a TAF-1 transactivation domain.

157. (New) The method of claim 155, wherein the transactivation domain is a VP-16 transactivation domain and wherein the DNA binding domain is a GAL-4 DNA binding domain.

158. (New) The method of claim 155, wherein the transactivation domain is a TAF-1 transactivation domain and wherein the DNA binding domain is a GAL-4 binding domain.

159. (New) The method of claim 144, wherein the molecular switch is tissue specific.

160. (New) The method of claim 159, wherein the tissue specificity of the molecular switch is controlled by a tissue-specific transactivation domain.

161. (New) The method of claim 159, wherein the second nucleic acid cassette comprising the target gene further comprises a tissue-specific cis-element.

162. (New) The method of claim 144, wherein the alternation is a deletion of carboxyl terminal amino acids in the mutated steroid hormone receptor superfamily ligand binding domain.

163. (New) The method of claim 144, wherein the ligand is RU38486.

164. (New) The method of claim 144, wherein the ligand is 11 beta-(4-dimethylaminophenyl)-17 beta-hydroxy-17 alpha-propinyl-4,9-estradiene-3-one.

165. (New) The method of claim 144, wherein the ligand is an antiprogesterone.

166. (New) The method of claim 144, wherein the ligand requires conversion to an active form in an end organ.

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167. (New) The method of claim 144, wherein the ligand has a side chain which increases or restricts solubility, membrane transfer or target organ accessibility.

168. (New) A method of regulating an transient expression of a desired protein or RNA in an animal *in vivo* comprising:

administering to the animal a pharmacological dose of a ligand that activates a molecular switch encoded by a molecule switch expression cassette comprised in the animal, wherein the molecular switch comprises a sequence specific DNA binding domain and mutated steroid hormone superfamily receptor ligand binding domain which is activated by the ligand which is not a native ligand for a corresponding wild type steroid hormone superfamily receptor ligand binding domain. and wherein the activation of the molecular switch results in binding to a specific DNA sequence in the regulatory region of a target gene promoter and results in the expression of the desired protein or RNA from the target gene.

169. (New) The method of claim 168, wherein the mutated steroid hormone superfamily receptor ligand binding domain is the ligand binding domain of a steroid hormone superfamily receptor selected from the group consisting of: estrogen; progesterone; glucocorticoid-α; glucocorticoid-β; mineralcorticoid; androgen; thyroid hormone; retinoic acid; retinoid X; Vitamin D; COUP-TF; ecdysone; Nurr-1 and orphan receptors.

170. (New) The method of claim 168, wherein the mutated steroid hormone superfamily receptor ligand binding domain is a mutated progesterone ligand binding domain and the ligand is an anti-progestin.

171. (New) The method of claim 170, wherein the anti-progestin is selected from the group consisting of: RU 38486; Org31806; and Org 31376.

172. (New) The method of claim 168, wherein DNA binding domain is a non-steroid hormone DNA binding domain.

173. (New) The method of claim 168, wherein the DNA binding domain is selected from the group consisting of: a GAL-4 DNA binding domain; a viral DNA binding domains; an insect DNA binding domains; and a non-mammalian DNA binding domains.

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174. (New) The method of claim 168, wherein the molecular switch further comprises a transactivation domain distinct from a steroid hormone receptor superfamily transactivation domain.

175. (New) The method of claim 168, wherein the transient expression is up-regulated.

176. (New) The method of claim 135, wherein the transient expression is down-regulated.

177. (New) A method of regulating a transient expression of a desired protein or RNA in an animal *in vivo*, the method comprising:

administering to the animal a pharmacological dose of a ligand, wherein the ligand is an antagonist for a non-mutated progesterone receptor protein,

wherein the animal comprises a coding sequence of a molecular switch comprising a mutated progesterone receptor protein, wherein the mutated progesterone receptor protein comprises:

a DNA binding domain specific for a DNA site on a promoter transcriptionally linked to a target gene;

a mutated progesterone receptor ligand binding domain which has a deletion of from 1 to 54 C-terminal amino acids and binds to and is activated by the ligand;

a transactivation domain which causes a transcription from the promoter when the molecular switch is bound to the promoter and the ligand; and

wherein administration of the ligand regulates expression of the desired protein or RNA from the target gene.

178. (New) The method of claim 177, wherein the DNA binding domain is a natural DNA binding domain, a non-native DNA binding domain, or a modified DNA binding domain.

179. (New) The method of claim 177, wherein the DNA binding domain is a GAL-4 DNA binding domain, a virus DNA binding domain, an insect DNA binding domain, or a non-mammalian DNA binding domain.

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180. (New) The method of claim 177, wherein the animal is a mammal.

181. (New) The method of claim 180, wherein the mammal is a human.

182. (New) The method of claim 177, wherein the ligand selected from the group consisting of 5α-pregnane-3,20-dione; 11β-(4-dimethylaminophenyl)-17β-hydroxy-17α-propinyl-4,9-estradiene-3-one; 11β-(4-dimethylaminophenyl)-17α-hydroxy-17β-(3-hydroxypropyl)-13α-methyl-4,9-gonadiene-3-one; 11β-(4-acetylphenyl)-17β-hydroxy-17α--(1-propinyl)-4,9-estradiene-3-one; 11β-(4-dimethylaminophenyl)-17β-hydroxy-17-α--(3-hydroxy-1(Z)-propenyl-estra-4,9-diene-3-one; (7β,11β,17β)-11-(4-dimethylaminophenyl)-7-methyl-4',5'-dihydrospiro(ester-4,9-diene-17,2'(3'H)-furan)-3-one; (11β,14β,17α)-4',5'-dihydro-11-(4-dimethylaminophenyl)- (spiroestra-4,9-diene-17,2'(3'H)-furan)-3-one.

183. (New) The method of claim 177 wherein the ligand is an anti-progesterone.

184. (New) The method of claim 183 wherein the antiprogesterone is RU 34846, Org 3186, or Org 31376.

185. (New) The method of claim 177, wherein the mutated progesterone receptor ligand binding domain binds to a compound selected from the group consisting of non-natural ligands, non-native hormones and anti-hormones.

186. (New) The method of claim 177, wherein the transactivation domain is selected from the group consisting of VP-16, TAF-1, TAF-2, and TAU-2.

187. (New) The method of claim 177, wherein the transactivation domain is a VP-16 transactivation domain and wherein the DNA binding domain is a GAL-4 DNA binding domain.

188. (New) The method of claim 177, wherein the transactivation domain is a TAF-1 transactivation domain and wherein the DNA binding domain is a GAL-4 binding domain.

189. (New) The method of claim 177, wherein the molecular switch is tissue specific.

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190. (New) The method of claim 189, wherein the tissue specificity of the molecular switch is controlled by a tissue-specific transactivation domain.

191. (New) The method of claim 190, wherein the target gene further comprises a tissue-specific cis-element.

192. (New) The method of claim 177, wherein the ligand has a side chain which increases or restricts solubility, membrane transfer or target organ accessibility.